

March 26, 2007

Teresa R. Borzcik
Regulatory Affairs Manager
Specialty Materials EHS&R
3M Center, Bldg. 236-1-10
St. Paul, MN 55144

Dear Ms. Borzcik:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the revised test plan and robust summaries for Perfluoro-compounds, C₅-C₁₈ dated June 18, 2003. EPA posted the revised submission on the ChemRTK HPV Challenge Program Web site on October 22, 2003. I commend 3M for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that 3M advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact me at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsc hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Mark W. Townsend, Chief
HPV Chemicals Branch

Enclosure

cc: O. Hernandez
C. Augustyniak
J. Willis

**EPA Comments on Chemical RTK HPV Challenge Submission:
Perfluorocompounds, C5-C18 Alkanes and Amines Category.**

SUMMARY OF EPA COMMENTS

The sponsor, 3M, submitted a revised test plan and robust summaries to EPA for the revised Perfluoro-compounds (PFCs), C5-C18 Alkanes and Amines category (CAS No. 86508-42-1) dated January 18, 2003. The category consists of 9 substances presented in two subcategories: the Alkane Subcategory of 4 substances and the Amine Subcategory of 5 substances

EPA has reviewed this submission and has reached the following conclusions:

1. Category Definition. The category is adequately defined.
2. Category Justification. The measured and estimated data submitted for physicochemical, environmental fate, and health endpoints support the grouping of the PFC alkanes and amines products into one category except for ecological effects, for which more supporting information is needed.
3. Physicochemical Properties. The submitter needs to provide melting point and solubility data for these chemicals; provide the vapor pressure values that were used to calculate the extrapolated values; and verify the accuracy of the partition coefficient value provided for CAS No. 311-89-7.
4. Environmental Fate. The submitter needs to enhance the technical discussion for stability in water of these substances, provide adequate biodegradation data for CAS No. 311-89-7 and additional biodegradation information for CAS No. 678-26-2, and provide additional fugacity data.
5. Health Effects. The submitted data are adequate for the acute, repeated-dose, and gene mutation toxicity endpoints for the purposes of the HPV challenge Program. Although the submitted data do not address all endpoints, EPA agrees with the submitter that the chemicals in this category appear to have low toxicity potential for these endpoints and the available data are sufficient to address the screening level endpoints for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.
6. Ecological Effects. As all of the acute and the one chronic test were conducted above their water solubility, testing needs to be performed on selected chemicals below or at their water solubility.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

**EPA COMMENTS ON THE PERFLUORO-COMPOUNDS, C5-C18 ALKANES AND AMINES
CATEGORY CHALLENGE SUBMISSION**

Category Definition

The submitter presents the category as two subcategories:

Perfluoroalkanes:

- (a) perfluoropentane (CAS No. 678-26-2)
- (b) perfluorohexane (CAS No. 355-42-0)
- (c) perfluoroheptane (CAS No. 335-57-9)
- (d) perfluorooctane (CAS No. 307-34-6)

Perfluoroamines:

- (a) perfluorotripropylamine (CAS No. 338-83-0)
- (b & c) **Ha/Hb** perfluorotributylamine (CAS No. 311-89-7)
- (d) perfluorotriamylamine (CAS No. 338-84-1)
- (e) perfluoro-N,N,N',N'-tetrapropylhexanediamine (CAS No. 143356-32-5)

All chemicals consist of branched, linear, and cyclic perfluorinated hydrocarbons or alkylamines having carbon numbers predominantly in the range of C5-C18 and boiling in the range of approximately 25 °C to 255 °C.

Category Justification

The measured and estimated data submitted for physicochemical, environmental fate, and health endpoints support the grouping of the PFC alkanes and amines products into one category.

PFC Alkanes

The submitter's rationale for grouping the PFC alkanes into a single subcategory is based on the structural similarity of the chemicals, the ultimate fate associated with the structures, similar physicochemical properties, and similar low mammalian toxicity. The submitter also indicated that this subcategory of chemicals is fully fluorinated and lacks functional groups, and therefore is chemically and biologically inert. EPA generally agrees with this position, but believes that the claim of biological inertness is unsupported with respect to ecological effects.

PFC Amines

The submitter's rationale for grouping the PFC amines into a single subcategory is based on the structural similarity of the chemicals, the ultimate fate associated with the structures, similar physical/chemical properties, and similar low mammalian toxicity. The submitter also indicated that this class of chemicals is fully fluorinated and does not contain functional "end groups", and thus is chemically and biologically inert. For mammalian toxicity, the data support this position.

The test plan does not address the properties of the amine function. The PFC amines test plan appears to be an exact copy of the PFC alkanes test plan, with minor changes to reflect the different names and available health effects data. The submitter needs to explain the assertion that the perfluorinated amines lack reactive functional groups. Normally, amino groups are reactive, and tertiary amines are strongly basic and corrosive. If amino group reactivity is altered/reduced by the perfluoro substitution, the submitter needs to specifically explain and reference these unusual properties. Otherwise, it seems unlikely that the perfluorinated alkanes and amines will be equally unreactive. This concern applies mainly to ecological effects, as it is not clear whether these amines are strong enough bases to cause toxic effects associated with amines, need to be neutralized to conduct testing, etc. Inclusion of existing measured pKa/pKb values of perfluoroalkylamines would help clarify these issues. The available ecotoxicity data are inadequate to support the submitter's position because of study inadequacies; other hydrophobic alkylamines are known to exhibit lethality to aquatic organisms at low concentrations.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data provided by the submitter for boiling point are adequate for the purposes of the HPV Challenge Program.

Melting point. The submitter indicates that this endpoint is not relevant because all materials in this class are in a liquid state. However, the submitter did not indicate the temperature above which these materials are liquids. Simply indicating that this endpoint is not relevant is not adequate for the purposes of the HPV Challenge Program and the submitter needs to provide melting point data for these chemicals. Data from published handbook sources are adequate, as long as the submitter provides the source. Calculated values are acceptable if under 0 °C.

Vapor pressure. The submitter needs to provide the vapor pressure values that were used to calculate the extrapolated values for these chemicals. Because perfluoro compounds do not follow linear temperature-vapor pressure relationships, extrapolations that are based on high temperature data may be in error.

Partition coefficient and water solubility. The calculated partition coefficients for PFC alkanes are adequate. The submitter needs to provide calculated partition coefficients for PFC amines as well. The submitter provided a measured Kow for perfluorotributylamine (CAS No. 311-89-7) of 557, which is equivalent to a log Kow of 2.75, and a measured water solubility value of 0.68 mg/L. These values are inconsistent because a chemical with a log Kow value of 2.75 should have a much higher water solubility value than the 0.68 mg/L value reported by the submitter. In turn, a chemical with a water solubility value of 0.68 mg/L should have a log Kow value much higher than 2.75. The submitter needs to address this apparent discrepancy.

In addition, the water solubility measurements were performed on two products and were not of adequate quality. Reported solubility of "<1 mg/ml" is also insufficient. Measured solubility is needed unless the value is below 1 ppb. The submitter needs to provide measured values for the category substances.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation are adequate for the purposes of the HPV Challenge Program.

Stability in water. EPA agrees with the submitter that these chemicals will not hydrolyze; however, it is not sufficient to indicate that these chemicals are highly volatile and insoluble. The submitter needs to incorporate, in the test plan and robust summaries, a brief statement indicating why these chemicals are not capable of undergoing hydrolysis, highlighting the lack of water-sensitive groups as appropriate.

Biodegradation. The biodegradation data provided by the submitter for CAS No. 311-89-7 are not adequate for the purposes of the HPV Challenge Program. The submitter indicates in the robust summary that the concentration of test solution is 10,000 mg Product Ha/L., and that the medium consists of BOD water inoculated with 6 mg/L stale sewage. This extreme test substance/biomass ratio makes it possible that microbial toxicity could account for the results. Furthermore, the submitter did not provide a description of the test method. The submitter needs to provide sound biodegradation data, preferably following OECD TG 301.

The biodegradation summary for Product A (CAS No. 678-26-2) needs to include results describing the Theoretical Oxygen Demand (ThOD), and information about the test solution and the medium.

Fugacity. For PFC alkanes, the fugacity data provided by the submitter for Product A (perfluoropentane) are adequate for the purposes of the HPV Challenge Program. However, because some of the higher carbon number perfluorinated alkanes, such as perfluorooctane, are liquids at room temperature, there is the possibility of release of these compounds into water or soil. Therefore, EPA recommends that the submitter incorporate fugacity models for these compounds showing releases to air, water, and soil.

For PFC amines, as most physicochemical and environmental fate data are for Product Ha (perfluorotributylamine), the submitter needs to include fugacity data for this chemical in the robust summary. Once the apparent discrepancy discussed above under *Partition coefficient and water solubility* is resolved, the submitter also needs to provide modeling data for the release of these

chemicals into water and soil.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

EPA considers the submitted data adequate for the purposes of the HPV Challenge Program. Although the data submitted for health effects do not address all endpoints, the chemicals in this category are unconventional. EPA believes that these chemicals will not be easily metabolized into toxic metabolites, as is apparent from the data indicating no toxicity to very low toxicity at high doses in the acute and repeated-dose toxicity studies for both subcategories.

The submitted data are adequate for acute and repeated-dose toxicity endpoints for the purposes of the HPV challenge Program. The submitter did not include data for the reproductive/developmental toxicity endpoints, but did provide an explanation, based on their chemically and biologically inactive nature, for not conducting these tests. EPA considers this reasoning supported for these chemicals by available data.

The submitter needs to address missing study details in the robust summaries.

PFC alkanes: *Genetic toxicity.* The submitter provided a robust summary for an attempted gene mutation assay, listing compound-related difficulties encountered during the assay. The submitter did not provide data for the chromosomal aberrations endpoint nor any explanation for the lack of data. The submitter should provide any such information available to permit an assessment of any difficulties testing these chemicals.

Reproduction toxicity. The submitter needs to provide information in robust summary format on the evaluation of reproductive organs from the 90-day inhalation study in rats to address this endpoint.

PFC amines: *Genetic toxicity.* The submitted data are adequate for gene mutation for the purposes of the HPV challenge Program. The submitter did not provide data for the chromosomal aberrations endpoints, but provided an explanation, based on their chemically and biologically inactive nature, for not conducting the test. EPA considers this reasoning supported by available data.

Ecological Effects (fish, invertebrates, and algae)

General. All aquatic toxicity endpoints were tested above their water solubility limit, and lack critical study details including pH, water hardness, temperature, and total chemical composition. EPA generally requests that hydrophobic chemicals of this type be tested at greater than or equal to 1 ppb, but clearly not exceeding the water solubility limit, at neutral pH, moderate water hardness, TOC < 2.0 mg/L, closed test system, zero head space, and using mean measured concentrations. Because of the lack of reliable measured solubilities for these substances and the question raised above about the reported Kow for Kow for perfluorotributylamine, the testing recommended below should be designed to reflect the measured and corrected values and other properties including basicity and volatility.

PFC alkanes. EPA disagrees with the submitter's recommendation that no further testing is necessary. These chemicals should be tested at or below the water solubility without filtering, using measured concentrations. EPA recommends that because the chemicals have high log Kows and low water solubility, only chronic testing (OECD TG 211) be conducted on CAS No. 678-26-2, at or below its water solubility limit. If toxicity is evident, then EPA suggests chronic daphnia testing on CAS No. 307-34-6 to clarify the category toxicity boundary. EPA requests that the submitter specify the amounts of perfluorinated ether or amine compounds present in the test substances, to better understand the test results. EPA regards any perfluorinated amine impurities as potentially toxic to aquatic organisms.

PFC amines. All aquatic endpoints were tested above their water solubility limit and lack major details including total organic carbon, total chemical composition, dissolved oxygen, pH, and water hardness.

Acute testing in fish, daphnid and algae (OECD TGS 203, 202, 201) should be performed at or below the reported water solubility limit, without filtering, and neutralized with HCl to pH 7 on the most water-soluble compound. EPA recommends that a chronic daphnia reproduction study be conducted on CAS Nos. 311-89-7 at no less than 1 ppb concentration or the chemical's water solubility limit. All testing should be conducted using mean measured concentrations and follow the additional test guidance noted above under "General." EPA requests that the submitter specify the amount of perfluorinated alkane and ether compounds that may be present as impurities in the final product, to better understand the test results.

Specific Comments on the Robust Summaries

Health Effects

Acute toxicity. For *PFC alkanes* the submitter needs to provide the appropriate reference for the acute oral toxicity study--the "Method/Guideline" reference provided is for the Dermal Irritation Study. For *PFC amines*, the purity information is lacking in all robust summaries.

Repeated-dose toxicity. For *PFC alkanes*, the robust summary for the 90-day inhalation study, the submitter needs to list hematology and biochemistry parameters evaluated, organs that were weighed, and a list of tissues and organs evaluated for macroscopic and microscopic pathology. For *PFC amines*, the robust summary for the subacute inhalation study, the submitter needs to list hematology and biochemistry parameters evaluated, organs that were weighed, and tissues and organs evaluated for macroscopic and microscopic pathology.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.